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Terms	Documents
L5 same (advantag$ or useful$)	5

Database: US Patents Full-Text Database; US Pre-Grant Publication Full-Text Database; JPO Abstracts Database; EPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L6

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DATE: Wednesday, July 31, 2002 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
	DB=USPT; PLUR=YES; OP=OR		
L6	L5 same (advantag$ or useful$)	5	L6
L5	L4 same (detect$ or indicat$ or identif$ or diagnos$)	38	L5
L4	metast$ near0 liver near0 cancer	115	L4
L3	L2 same differen$	6	L3
L2	L1 same metasta$	97	L2
L1	hepatocellular near0 carcinoma	1118	L1

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 13:25:20 ON 31 JUL 2002)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 13:25:40 ON 31 JUL 2002

L1 71 S COLON(W)CANCER(W)LIVER(W)METASTASIS
L2 4 S L1 (P)IDENTIFICATION (P)DIFFERENTIALLY
L3 1 DUPLICATE REMOVE L2 (3 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 13:27:12 ON 31 JUL 2002

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Search Results -

Terms	Documents
metasta$ same liver same trypsin	5

Database: US Patents Full-Text Database
US Pre-Grant Publication Full-Text Database
JPO Abstracts Database
EPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search: L6

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Recall Text | Clear

Search History

DATE: Wednesday, July 31, 2002 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=OR			
L6	metasta$ same liver same trypsin	5	L6
L5	L1 same inhibitor$	4	L5
L4	L1 same trypsin	0	L4
L3	L1 same psti	0	L3
L2	L1 same trypsin same inhibitor$	0	L2
L1	metasta$ near0 liver near0 cancer$	114	L1

END OF SEARCH HISTORY

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L5: Entry 1 of 4 File: USPT

DOCUMENT-IDENTIFIER: US 6235493 B1
TITLE: Amino acid substituted-cresyl violet, synthetic fluorogenic substrates for the analysis of agents in individual in vivo cells or tissue

Brief Summary Text (20):
14. C. F. Sier, et al. 1994. Inactive urokinase and increased levels of its inhibitor type 1 in colorectal cancer liver metastasis. Gastroenterology, 107, 1449-56.

Detailed Description Text (12):
The extracellular action of cathepsin B is an early step in the proteolytic cascade involved in metastasis by activation of proforms of plasminogen activators and matrix metalloproteinases that are present in the extracellular space. Proteases are synthesized in an inactive proform or preproform and need to be activated for example by cleavage by other proteases before they are able to degrade proteins (37,38,39). Therefore, the role of cathepsin B in an in vivo rat model of colon cancer metastasis in the liver was established. Metastasis was mimicked by administration of rat colon cancer cells in the portal vein of rats. We tested whether development of metastases could be inhibited by treatment of the animals with a selective non-toxic water-soluble small molecular inhibitor of cathepsin B, Mu-Phe-homoPhe-fluoro-methylketone (FMK) (40,41). First, the localization of cathepsin B and its activity at the plasma membrane of the cancer cells was investigated. For this purpose, a new synthetic fluorogenic substrate for cathepsin B, [Z-Arg].sup.2 -cresyl violet was developed, which permits the localization of its activity in living cells with the use of confocal scanning laser microscopy (CSLM). The use of living cells was considered to be of vital importance because activity of proteases in vivo is determined by activation of the proforms, suppression by endogeneous inhibitors (6,30,42) and the cellular microenvironment of the enzyme (39). This is particularly relevant for cathpsin B which normally functions at acidic pH in the lysosomes, whereas the extracellular pH is slightly alkaline (43).

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      (FILE 'HOME' ENTERED AT 09:48:56 ON 31 JUL 2002)

      FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE' ENTERED AT 09:49:13 ON 31 JUL 2002
L1           316 S EXPRESS? (P)PANCREA? (P)TRYPSIN (P)INHIBITOR? (P)GENE?
L2             4 S L1 (P)NEOPLASTIC (P)TISSUE?
L3            24 S L1 (P)LIVER?
L4             1 S L3 (P)METASTA?(P)CANCER?

=> s l3 (p)cancer?
L5             1 L3 (P) CANCER?

=>
```

light chain (ITI-LC, also known as bikunin or urinary **trypsin inhibitor**) was examined in various human tissues. By reverse-transcription polymerase chain reaction, the mRNA was detected not only in the **liver**, a known site of ITI-LC production, but also in the kidney, heart, lung, and **pancreas**. By RNA blot analysis, the mRNA was also detected in the **pancreas** and **liver**, but not in the kidney, heart, or lung. The ITI-LC protein was immunohistochemically detected along the surface of **pancreatic** acinar cells. These results indicate the apparent **expression** of the **gene** for ITI-LC in the **pancreas**. ITI-LC protein on the surface of **pancreatic** acinar cells may play an important role in preventing autodigestion by exocrine enzymes such as trypsinogen and chymotrypsinogen.

L6 ANSWER 5 OF 8 MEDLINE DUPLICATE 4
AN 96032548 MEDLINE
DN 96032548 PubMed ID: 7556646
TI **Pancreatic** secretory **trypsin inhibitor** **gene** is highly **expressed** in the **liver** of adult-onset type II citrullinemia.
AU Kobayashi K; Nakata M; Terazono H; Shinsato T; Saheki T
CS Department of Biochemistry, Faculty of Medicine, Kagoshima University, Japan.
SO FEBS LETTERS, (1995 Sep 18) 372 (1) 69-73.
Journal code: 0155157. ISSN: 0014-5793.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199511
ED Entered STN: 19951227
Last Updated on STN: 19980206
Entered Medline: 19951106
AB Deficiency of argininosuccinate synthetase (ASS) causes citrullinemia. Type II citrullinemia is found in most patients with adult-onset citrullinemia in Japan, and ASS is deficient specifically in the **liver**. Previous studies have shown that the decrease of hepatic ASS activity is caused by a decrease in enzyme protein with normal kinetic properties and that there are no apparent abnormalities in the amount, translational activity, and nucleotide sequence of hepatic ASS mRNA. Recent results of homozygosity testing indicate that the primary defect of type II citrullinemia is not within the ASS **gene** locus. In this present work, to understand the pathogenesis and pathophysiology of type II citrullinemia, we have characterized the alterations of **gene** **expression** in the **liver** of type II patients using the recently developed mRNA differential display method. Some cDNA bands **expressed** differently in type II citrullinemia patients and control were selected, cloned, and sequenced. Nucleotide sequence analysis and homology searching revealed an interesting clone which has 99% homology with the human **pancreatic** secretory **trypsin** **inhibitor** (hPSTI). Northern blot and RT-PCR analyses showed that the **expression** of hPSTI mRNA increased significantly in the **liver** of all type II patients tested. Furthermore, the concentration of hPSTI protein was found to be higher in the **liver** of type II citrullinemia than in control. These results suggest that hPSTI

Monden, Morito; Mori, Takesada; Ogawa, Michio; Matsubara, Kenichi
CS Inst. Mol. Cell. Biol., Osaka Univ., Osaka, Japan
SO Int. J. Cancer (1993), 55(5), 728-34
CODEN: IJCNAW; ISSN: 0020-7136
DT Journal
LA English
AB Twenty hepatocellular carcinomas (HCC) were analyzed by Northern blotting to test the expression of pancreatic secretory trypsin inhibitor (PSTI). This gene was expressed in all HCCs, but not in other tumors, including mammary, thyroid, pulmonary and ovarian cancers. Some gastric and colonic cancers weakly expressed PSTI. Among cell lines examd. in a similar manner, PSTI was expressed in all of 4 derived from hepatoma. On the other hand, among 15 cell lines derived from cancers other than hepatoma, only 3, derived from pancreatic, colonic and gastric cancers, weakly expressed PSTI. A CAT assay using a deletion set of the 5' region from the cloned PSTI gene has shown that in hepatoma cell lines, the expression of this gene is dependent on the presence of 2 regulatory regions that include an IL-6 responsive element and an Ap-I-binding site. However, in non-hepatoma cell lines, the 2 regulatory regions are not necessary for expression. The blood level of PSTI in 27 patients with HCC was significantly increased, and it was pos. correlated with tumor size, suggesting that specific expression of PSTI in HCC causes this effect and that elevated blood level of PSTI without inflammation indicates the presence of HCC.

L6 ANSWER 8 OF 8 MEDLINE DUPLICATE 6
AN 89322236 MEDLINE
DN 89322236 PubMed ID: 2751646
TI On the cDNA's for two types of rat pancreatic secretory trypsin inhibitor.
AU Horii A; Tomita N; Yokouchi H; Doi S; Uda K; Ogawa M; Mori T; Matsubara K
CS Institute for Molecular and Cellular Biology, Osaka University, Suita, Japan.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1989 Jul 14) 162 (1) 151-9.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-M27882; GENBANK-M27883
EM 198908
ED Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890814
AB Two types of cDNA, which code for the two types of rat **pancreatic** secretory **trypsin inhibitors** (PSTIs), were cloned and sequenced. Both predicted amino acid sequences consisting of 79 amino acids, with the secretion signal peptide consisting of 18 and 23 amino acids for PSTI-I and PSTI-II, respectively. The nucleotide sequences were 91% homologous between the two cDNAs, but 68% and 65% homologous, respectively, when compared with human PSTI cDNA. Northern blot analyses showed that PSTI-I is **expressed** in the **pancreas**, whereas PSTI-II is **expressed** in the **pancreas** and the **liver** using the same promoter. Southern blot analyses suggested that both PSTI-I and PSTI-II **genes** are single copy **genes** per haploid genome. Duplication of rat PSTI **gene** seems to have

occurred recently, after the divergence of humans and rats.

=>

L6 ANSWER 8 OF 8 MEDLINE DUPLICATE 6
AN 89322236 MEDLINE
DN 89322236 PubMed ID: 2751646
TI On the cDNA's for two types of rat pancreatic secretory trypsin inhibitor.
AU Horii A; Tomita N; Yokouchi H; Doi S; Uda K; Ogawa M; Mori T; Matsubara K
CS Institute for Molecular and Cellular Biology, Osaka University, Suita, Japan.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1989 Jul 14) 162 (1) 151-9.
Journal code: 0372516. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-M27882; GENBANK-M27883
EM 198908
ED Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19890814
AB Two types of cDNA, which code for the two types of rat **pancreatic** secretory **trypsin inhibitors** (PSTIs), were cloned and sequenced. Both predicted amino acid sequences consisting of 79 amino acids, with the secretion signal peptide consisting of 18 and 23 amino acids for PSTI-I and PSTI-II, respectively. The nucleotide sequences were 91% homologous between the two cDNAs, but 68% and 65% homologous, respectively, when compared with human PSTI cDNA. Northern blot analyses showed that PSTI-I is **expressed** in the **pancreas**, whereas PSTI-II is **expressed** in the **pancreas** and the **liver** using the same promoter. Southern blot analyses suggested that both PSTI-I and PSTI-II **genes** are single copy **genes** per haploid genome. Duplication of rat PSTI **gene** seems to have occurred recently, after the divergence of humans and rats.

L6 ANSWER 3 OF 8 MEDLINE DUPLICATE 2
AN 1998173549 MEDLINE
DN 98173549 PubMed ID: 9514613
TI Gene expression of the two heavy chains and one light chain forming the inter-alpha-trypsin-inhibitor in human tissues.
AU Mizushima S; Nii A; Kato K; Uemura A
CS Biosciences Research Laboratory, Mochida Pharmaceutical Co., Ltd., Tokyo, Japan.
SO BIOLOGICAL AND PHARMACEUTICAL BULLETIN, (1998 Feb) 21 (2) 167-9.
Journal code: 9311984. ISSN: 0918-6158.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980430
Last Updated on STN: 19980430
Entered Medline: 19980420
AB Human inter-alpha-**trypsin-inhibitor** (ITI) is a serine proteinase **inhibitor** with a molecular weight of 220 kDa which consists of 3 different polypeptides. The constitutive components are 2 heavy chains (H1 and H2 chains) and 1 light chain (L chain), and its **inhibitory** activity is considered to be derived from this L chain. It has also been reported that this L chain is almost identical to the **trypsin inhibitor** (UTI) occurring in human urine. We examined the **gene expression** of the ITI constitutive peptides in human tissues using the reverse transcription (RT) -PCR technique. As a result, the **genes** of the H1 chain were found to be **expressed** in various tissues, particularly strongly in the **liver**. On the other hand, the **genes** of the H2 chain were found to be strongly **expressed** in the adrenal glands, brain, kidneys, and lungs, as well as the **liver**. Further, the PCR amplification product of the L chain was strongly detected not only in the **liver** but also in the **pancreas**, kidneys, lungs, stomach and testes. These results suggest the possibility that the major tissue which produces ITI is the **liver**, and the H chains and L chain (UTI) are produced as a component of ITI- related proteins in other tissues as well as in the **liver**.

L6 ANSWER 4 OF 8 MEDLINE DUPLICATE 3
AN 97044739 MEDLINE
DN 97044739 PubMed ID: 8889810
TI Expression of inter-alpha-trypsin inhibitor light chain (bikunin) in human pancreas.
AU Itoh H; Tomita M; Kobayashi T; Uchino H; Maruyama H; Nawa Y
CS Department of Parasitology, Miyazaki Medical College.
SO JOURNAL OF BIOCHEMISTRY, (1996 Aug) 120 (2) 271-5.
Journal code: 0376600. ISSN: 0021-924X.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199704
ED Entered STN: 19970422
Last Updated on STN: 19970422
Entered Medline: 19970408
AB **Expression** of inter-alpha-**trypsin inhibitor**